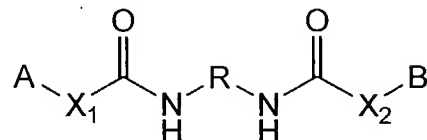


WHAT IS CLAIMED IS:

1. A method of forming a bioconjugate compound of the formula:



wherein:

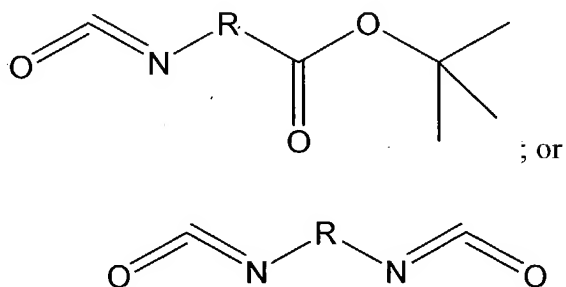
A is an active agent moiety;

B is a biopolymer moiety;

X<sub>1</sub> and X<sub>2</sub> are independently N or O; and

R is substituted alkylene or unsubstituted alkylene or unsubstituted or substituted heteroalkylene, wherein said R moiety is from 1 to about 30 atoms in length;  
said method comprising:

contacting one of an A precursor or a B precursor, wherein the A precursor and the B precursor independently comprise an active hydroxy or amino functionality, with a bifunctional isocyanate compound of one of the following formulae:

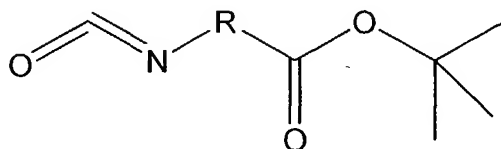


under reaction conditions wherein the isocyanate functional group covalently reacts with the hydroxy or the amino group of the A precursor or the B precursor to form a first reaction product; and then

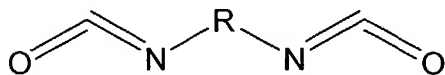
contacting the other of A precursor or the B precursor with the first reaction product under reaction conditions wherein the first reaction product reacts with the other of the A precursor or the B precursor to form the bioconjugate compound.

2. A method according to claim 1, wherein said active agent is a drug.

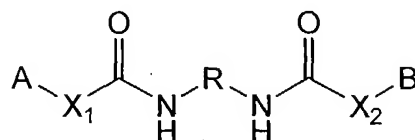
3. A method according to claim 1, wherein said biopolymer is a protein.
4. A method according to claim 1, wherein A is contacted with the bifunctional isocyanate moiety to form the first reaction product.
5. A method according to claim 1, wherein B is contacted with the bifunctional isocyanate moiety to form the first reaction product.
6. A method according to claim 1, wherein  $X_1$  is O.
7. A method according to claim 1, wherein  $X_1$  is N.
8. A method according to claim 1, wherein  $X_2$  is O.
9. A method according to claim 1, wherein  $X_2$  is N.
10. A method according to claim 1, wherein R is from 1 to about 10 atoms in length.
11. A method according to claim 1, wherein R is  $-(CH_2O)_nCH_2-$  and n is from 1 to about 15.
12. A method according to claim 1, wherein R is  $-(CH_2CH_2O)_nCH_2-$  and n is from 1 to about 10.
13. A method according to claim 1, wherein R is from 3-7 atoms in length.
14. A method according to claim 1, wherein the bifunctional isocyanate compound is a compound of the formula:



15. A method according to claim 1, wherein the bifunctional isocyanate compound is a compound of the formula:



16. A method according to claim 1, wherein the biopolymer is p97.
17. A method according to claim 2, wherein the p97 is recombinant.
18. A method according to claim 1, wherein the active agent is a drug.
19. A method according to claim 1, wherein the drug is an antineoplastic agent.
20. A method according to claim 18, wherein the drug is camptothecin, 10-hydroxycamptothecin, taxol, or doxorubicin.
21. A method according to claim 18, wherein the drug is useful for treating a disorder of the central nervous system.
22. A method according to claim 1, wherein the active agent is an enzyme.
23. A method according to claim 16, wherein the active agent is an enzyme.
24. A method according to claim 18, wherein the drug is a drug of less than 1000 daltons.
25. A method according to claim 18, wherein the drug is a drug of less than 400 daltons.
26. A bioconjugate compound of the formula:



wherein:

- A is an active agent moiety;
- B is a biopolymer moiety;
- X<sub>1</sub> and X<sub>2</sub> are independently N or O; and
- R is substituted alkylene or unsubstituted alkylene or unsubstituted or substituted heteroalkylene from 1 to about 30 atoms in length.

27. A compound according to claim 26, wherein said active agent is labeled.

28. A compound according to claim 26, wherein said biopolymer is a protein.
29. A compound according to claim 26, wherein  $X_1$  is O.
30. A compound according to claim 26, wherein  $X_1$  is N.
31. A compound according to claim 26, wherein  $X_2$  is O.
32. A compound according to claim 26, wherein  $X_2$  is N.
33. A compound according to claim 26, wherein R is from 1 to about 10 atoms in length.
34. A compound according to claim 26, wherein R is  $-(CH_2O)_nCH_2-$  and n is from 1 to about 15.
35. A compound according to claim 26, wherein R is  $-(CH_2CH_2O)_nCH_2-$  and n is from 1 to about 10.
36. A compound according to claim 26, wherein R is from 3-7 atoms in length.
37. A compound according to claim 26, wherein the biopolymer is p97.
38. A compound according to claim 26, wherein the active agent is a drug.
39. A compound according to claim 26, wherein the drug is an antineoplastic agent.
40. A compound according to claim 39, wherein the drug is camptothecin, 10-hydroxycamptothecin, taxol, or doxorubicin.
41. A compound according to claim 38, wherein the drug is useful for treating a disorder of the central nervous system.
42. A compound according to claim 26, wherein the active agent is an enzyme.
43. A compound according to claim 37, wherein the active agent is aldurazyme.
44. A compound according to claim 38, wherein the drug is a drug of less than 1000 daltons.

45. A compound according to claim 38, wherein the drug is a drug of less than 400 daltons.
46. A composition comprising a compound of any one of claims 26-45 and a pharmacologically acceptable excipient.
47. A method of treating a subject, said method comprising administering to said subject a composition according to claim 46.
48. A method according to claim 47, wherein said administering is by an intravenous, oral, intraperitoneal, dermal or rectal route.
49. A compound according to claim 26, wherein the bioconjugate further comprises a label.
50. A compound according to claim 26, wherein the bioconjugate is SYN027.
51. A bioconjugate, comprising p97 covalently linked via an amide moiety to a PEG chain of up to 50 atoms in length which is in turn coupled via a carbamate moiety to an alkyl chain of from 1-15 atoms in length which is in turn linked via a carbamate moiety to a first active agent.
52. A bioconjugate according to claim 51, wherein PEG is PEG4-10.
53. A bioconjugate according to claim 51, wherein the alkyl is homoalkyl from 3 to 10 atoms long.
54. A bioconjugate according to claim 51, wherein the first active agent is 10-hydroxycamptothecin.
55. A bioconjugate according to claim 51, wherein the bioconjugate comprises at least one other covalent linkage via an amide moiety to a PEG chain of up to 50 atoms in length which is in turn coupled via a carbamate moiety to an alkyl chain of from 1-15 atoms in length which is in turn linked via a carbamate moiety to a second active agent.
56. A bioconjugate according to claim 55, wherein the first and second active agents are the same or different, and if different, are useful in treating the same disease or condition.